METHOD AND APPARATUS FOR MULTISPRAY EMITTER FOR MASS SPECTROMETRY

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0001] This invention was made with Government support under Contract DE-AC0676RLO1830 awarded by the U.S. Department of Energy. The Government has certain rights in the invention.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0002] Not Applicable

BACKGROUND OF THE INVENTION

[0003] Various types of micro-fabricated devices have been used in the fields of chemical separations and analysis including capillary electrophoresis, capillary isoelectric focusing and nano column separations (where both flow channel and stationary phase supporting particles can be directly fabricated on chip). As electrospray ionization mass spectrometry (ESI-MS) has become a widely used analytical technique, considerable efforts have been directed at the development of interfaces for chip-based devices with electrospray ionization mass spectrometers. Examples of the current available interfaces include an open channel interface. For example, Zhang, B.; Liu, H.; Karger, B. L.; Foret, F. *Anal. Chem.* 1999, 71, 3258-3264 shows an electrospray with modifications, while Ramsey, R. S.; Ramsey, J. M. *Anal. Chem.* 1997, 69, 1174-1178 and Xue, Q.; Foret, F.; Dunayevskiy, Y. M.; Zavracky, P. M.; Mcgruer, N. E.; Karger, B. L. *Anal. Chem.* 1997, 69, 426-430 show an electrospray without modifications, where an electrospray was generated directly from the open channel terminus, attaching a fused-silica capillary to the channel end where the joint was either sealed, as shown in Licklider, L.; Wang, X.; Desai, A.; Tai, Y.; Lee, T. D. *Anal. Chem.* 2000, 72, 367-375, Figeys, D.; Ning, Y.; Aebersold, R. *Anal Chem.* 1997, 69, 3153-3160, and Bings, N. H.; Wang, C.; Skinner, C. D.; Colyer, C. L.; Thibault, P.; Harrison, D. J. *Anal. Chem.* 1999, 71, 3292-3296, or made by a liquid junction, as shown in Forest, F.; Zhou, H.; Gangl, E.; Karger, B. L. *Electrophoresis* 2000, 21, 1363-1371 and Zhang, B.; Foret, F.; Karger, B. L. *Anal. Chem.* 2000, 72, 1015-1022. These, and all other references described herein, including without limitation patents, technical papers, or otherwise, are incorporated in their entirety by this reference.

[0004] Despite these advances, the reliability and/or ease of fabrication of these interfaces still presents significant problems for their broad applicability. Ideally the interface of a microfabricated device with a mass spectrometer should integrate the electrospray emitter with the device to form a complete separation and electrospray unit that can be readily replicated. As described in the paper "A Fully Integrated Monolithic Mircrochip Electrospray Device for Mass Spectrometry, *Analytical Chemistry*, Vol. 72, No. 17, Sep. 1, 2000, 4058-4063, Schultz and Corso recently described a concept for a microfabricated electrospray emitter array where photolithographic patterning and plasma etching were used to fabricate an array of electrospray emitters on a silicon wafer. The technique offered a potential solution to the problem of system integration for high-throughput applications where each spray nozzle can be connected to a different sample well and operated sequentially. A limitation associated with the use of silicon technology for electrospray emitter fabrication, as reported by Schultz and Corso, is that each spray nozzle array can only be used reliably for a little more than 1 h. Also, each nozzle in the array described by Schultz and Corso is designed to be interfaced with both the analyte source and the entrance to the mass spectrometer sequentially. As such, the device does not utilize the array to impact the analyte throughput, or the resulting signal strength, in the mass spectrometer. This is an important drawback, as generating a higher total ion current, given a liquid flow rate, is an important objective for enhancing the sensitivity of mass spectrometers.

[0005] Thus, there exists a need for improved interfaces between chip based separation and analysis devices with electrospray ionization mass spectrometers, and a particular need for improved devices which enhance the total ion current given a liquid flow rate.

BRIEF SUMMARY OF THE INVENTION

[0006] Accordingly, it is an object of the present invention to provide a method and apparatus that increases the total ion current introduced into an electrospray ionization mass spectrometer, given a liquid flow rate of a sample. This objective is accomplished by use of the surprising discovery that an array of spray emitters directed into a mass spectrometer produce a greater total ion current than a single emitter having the same liquid flow rate. Due to the small size of the emitters commonly deployed in mass spectrometry, the present invention is most conveniently constructed as an array of spray emitters fabricated on a single chip, however, the present invention should be understood to encompass any apparatus wherein two or more emitters are simultaneously utilized to form an electrospray of a sample that is then directed into a mass spectrometer.

[0007] When fabricated as a single chip, the array of spray emitters is interfaced with a liquid sample source, including but not limited to liquid separation devices, on one side of the chip. Suitable liquid separation devices include, but are not limited to capillary electrophoresis devices, capillary isoelectric focusing devices, and nano column separation devices. Typically, while not meant to be limiting, the liquid sample is interfaced with the chip by providing a single reservoir for the sample that is common to all of the spray emitters. However, in certain applications, it may be preferred to provide a separate reservoir for each emitter, or a plurality of reservoirs common, each feeding a portion of the emitters.

[0008] The other side of the chip is interfaced with the entrance to a mass spectrometer. Liquid samples are passed through the array, whereupon the samples are formed into an electrospray at each spray emitter within the array. The total electrospray formed at all of the spray emitters are then simultaneously introduced into a mass spectrometer. Preferably, while not meant to be limiting, the total electrospray is introduced into the mass spectrometer through a multi-capillary inlet, as more fully described in U.S. patent application Ser. No. 09/860,727 filed May 18, 2001, entitled "Improved Ionization Source Utilizing a Multi-Capillary Inlet and Method of Operation" by Smith et al. While not meant to be limiting, those skilled in the art will better